	L #	Hits	Search Text	DBs	Time Stamp
1	L1	327	methionine adj aminopeptidase$	USPAT; US-PGPUB	2003/08/01 10:32
2	L2	5548	(methionine or met) same muta$10	USPAT; US-PGPUB	2003/08/01 10:33
3	L3	147	1 same 2	USPAT; US-PGPUB	2003/08/01 10:33

US-PAT-NO: 6403076

DOCUMENT-IDENTIFIER: US 6403076 B1

TITLE: Compositions for increasing hematopoiesis with interleukin-3 mutants

DATE-ISSUED: June 11, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bauer; S. Christopher	New Haven	MO	63068	N/A
Abrams; Mark Allen	St. Louis	MO	63130	N/A
Braford-Goldberg; Sarah Ruth	St. Louis	MO	63108	N/A
Caparon; Marie Helena	Chesterfield	MO	63017	N/A
Easton; Alan Michael	Maryland Heights	MO	63146	N/A
Klein; Barbara Kure	St. Louis	MO	63131	N/A
McKearn; John Patrick	Glencoe	MO	63038	N/A
Olins; Peter Q	Glencoe	MO	63038	N/A
Paik; Kumnan	Ballwin	MO	63021	N/A
Thomas; John Warren	Town & Country	MO	63131	N/A

APPL-NO: 08/ 468683

DATE FILED: June 6, 1995

PARENT-CASE:

This is a divisional of U.S. Ser. No. 08/191,973, filed Feb. 4, 1994, now U.S. Pat. No. 5,772,992; and is a continuation-in-part of U.S. Ser. No. 08/411,796, filed Apr. 6, 1995, now U.S. Pat. No. 5,677,149; which is a 371 of PCT/US93/11198, filed Nov. 22, 1993; which is a continuation-in-part of U.S. Ser. No. 07/981,044, filed Nov. 24, 1992, now abandoned.

US-CL-CURRENT: 424/85.2, 424/85.1 , 514/2 , 530/351

ABSTRACT:

The present invention relates to human interleukin-3 (hIL-3) variant or mutant proteins (muteins) functionally co-administered with a other colony stimulating factors (CSF), cytokines, lymphokines, interleukins, hematopoietic growth factors or IL-3 variants.

22 Claims, 1 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 1

---------- KWIC ---------

Detailed Description Text - DETX (31):

Suitable cells or cell lines for the production of the proteins claimed in the present invention may be bacterial cells. For example, the various strains of E. coli are well-known as host cells in the field of biotechnology. Examples of such strains include E. coli strains JM101 [Yanish-Perron, et al. (1985)] and MON105 [Obukowicz, et al. (1992)]. Also included in the present invention is the expression of the IL-3 variant protein utilizing a chromosomal expression vector for E. coli based on the bacteriophage Mu (Weinberg et al., 1993). Various strains of B. subtilis may also be employed as host cells for expression of the polypeptides of the present invention. Many strains of yeast cells known to those skilled in the art are also available as host cells for expression of the polypeptides of the present invention. When expressed in the E. coli cytoplasm, the above-mentioned **mutant** hIL-3 variants of the present invention may also be constructed with **Met**-Ala- at the N-terminus so that upon expression the **Met** is cleaved off leaving Ala at the N-terminus. The IL-3 variant proteins of the present invention may include polypeptides having **Met**-, Ala- or **Met**-Ala- attached to the N-terminus. When the IL-3 variant polypeptides are expressed in the cytoplasm of E. coli, polypeptides with and without **Met** attached to the N-terminus are obtained. The N-termini of proteins made in the cytoplasm of E. coli are affected by posttranslational processing by **methionine aminopeptidase** (Ben-Bassat et al., 1987) and possibly by other peptidases. These IL-3 variant proteins may also be expressed in E. coli by fusing a signal peptide to the N-terminus. This signal peptide is cleaved from the polypeptide as part of the secretion process. Secretion in E. coli can be used to obtain the correct amino acid at the N-terminus (e.g., Asn.sup.15 in the (15-125) hIL-3 polypeptide) due to the precise nature of the signal peptidase. This is in contrast to the heterogeneity which may be observed at the N-terminus of proteins expressed in the cytoplasm in E. coli.

US-PAT-NO: 6130318

DOCUMENT-IDENTIFIER: US 6130318 A

TITLE: hIL-4 mutant proteins used as antagonists or partial agonists of human interleukin 4

DATE-ISSUED: October 10, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wild; Hanno	Wuppertal	N/A	N/A	DE
Hanko; Rudolf	Dusseldorf	N/A	N/A	DE
Dorschug; Michael	Heiligenhaus	N/A	N/A	DE
Horlein; Hans-Dietrich	Wuppertal	N/A	N/A	DE
Beunink; Jurgen	Wuppertal	N/A	N/A	DE
Apeler; Heiner	Wuppertal	N/A	N/A	DE
Wehlmann; Hermann	Wuppertal	N/A	N/A	DE
Sebald; Walter	Wurzburg	N/A	N/A	DE

APPL-NO: 08/ 765012

DATE FILED: December 19, 1996

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
DE	44 23 131	July 1, 1994

PCT-DATA:
APPL-NO: PCT/EP95/02358
DATE-FILED: June 19, 1995
PUB-NO: WO96/01274
PUB-DATE: Jan 18, 1996
371-DATE: Dec 19, 1996
102(E)-DATE:Dec 19, 1996

US-CL-CURRENT: 530/351, 424/85.1 , 424/85.2

ABSTRACT:

The present invention relates to novel hIL-4 mutant proteins, to processes for preparing them, and to their use as medicaments, in particular in overshooting, falsely regulated immune reactions and autoimmune diseases.

12 Claims, 1 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 1

---------- KWIC ---------

Detailed Description Text - DETX (94):

In order to prepare an IL-4 mutein which lacks the N-terminal **methionine,** an amino acid was inserted, in position (+2), which leads to the elimination of the N-terminal **methionine,** in E. coli, by means of a specific **methionine aminopeptidase** (Flinta et al., Eur. J. Biochem. 15, 193-196, 1986). For this, the vector RPR9-IL4-Y 124D (enclosure 1) was cut with the restriction endonucleases XhoI and BamHI. The resulting DNA fragment of approx. 450 bp in length, which carries the sequence information for the IL4Y124D gene and a short (approx. 50 bp) fragment from the atpE region of the vector, was purified by agarose gel electrophoresis and recloned into the vector M13mp18, which had been cut with SalI and BamHI. Single-stranded DNA was prepared and subjected to an in-vitro **mutagenesis** reaction using the following oligonucleotide:

	Document ID	Issue Date	Pages	Title
1	US 20030144228 A1	20030731	74	PON3 and uses thereof
2	US 20030143680 A1	20030731	13	Descendants of bacteria devoid of N terminal formylation useful for the production of proteins and peptides
3	US 20030143595 A1	20030731	72	Hedgehog interacting proteins and uses related thereto
4	US 20030119729 A1	20030626	77	METHOD OF TREATING DOPAMINERGIC AND GABA-NERGIC DISORDERS
5	US 20030108916 A1	20030612	58	Cloning and functional assays of Xenopus ATR
6	US 20030105002 A1	20030605	104	RGS compositions and therapeutic and diagnostic uses therefor
7	US 20030104995 A1	20030605	64	Neuroprotective methods and compositions
8	US 20030104970 A1	20030605	70	Regulation of epithelial tissue by hedgehog-like polypeptides, and formulations and uses related thereto
9	US 20030100489 A1	20030529	59	Cell-cycle regulatory proteins, and uses related thereto
10	US 20030097676 A1	20030522	113	Plant acyl-CoA synthetases
11	US 20030097666 A1	20030522	274	Novel human genes and gene expression products:II
12	US 20030083242 A1	20030501	83	METHODS AND COMPOSITIONS FOR TREATING OR PREVENTING PERIPHERAL NEUROPATHIES

	Document ID	Issue Date	Pages	Title
13	US 20030082620 A1	20030501	59	Novel human genes and gene expression products: II
14	US 20030077587 A1	20030424	68	Glaucoma therapeutics and diagnostics
15	US 20030077288 A1	20030424	42	Compositions and methods for treatment of muscle wasting
16	US 20030073116 A1	20030417	97	ADAMTS13 genes and proteins and variants, and uses thereof
17	US 20030068831 A1	20030410	47	Proteins and druggable regions of proteins
18	US 20030068651 A1	20030410	49	Multi-target analysis of gene families for chemistry of high affinity and selective small molecules and other therapeutics
19	US 20030068650 A1	20030410	48	Target analysis for chemistry of specific and broad spectrum anti-infectives and other therapeutics
20	US 20030054437 A1	20030320	121	VERTEBRATE EMBRYONIC PATTERN-INDUCING PROTEINS AND USES RELATED THERETO
21	US 20030037357 A1	20030220	104	Plant acyl-CoA synthetases
22	US 20030028915 A1	20030206	38	Acyl coenzyme a thioesterases
23	US 20030022170 A1	20030130	59	Novel fibroblast growth factors and therapeutic and diagnostic uses therefor
24	US 20020197616 A1	20021226	175	Nod2 nucleic acids and proteins
25	US 20020182701 A1	20021205	46	Dominant negative variants of methionine aminopeptidase 2 (MetAP2) and clinical uses thereof
26	US 20020160375 A1	20021031	36	Human Patched genes and proteins, and uses related thereto
27	US 20020156239 A1	20021024	40	EPH receptor ligands, and uses related thereto

	Document ID	Issue Date	Pages	Title
28	US 20020151460 A1	20021017	72	REGULATION OF EPITHELIAL TISSUE BY HEDGEHOG-LIKE POLYPEPTIDES, AND FORMULATIONS AND USES RELATED THERETO
29	US 20020146773 A1	20021010	65	"Signalin" family of TGFbeta signal transduction proteins, and uses related thereto
30	US 20020144298 A1	20021003	50	Novel human genes and gene expression products
31	US 20020127687 A1	20020912	17	Genome DNA of bacterial symbiont of aphids
32	US 20020127673 A1	20020912	90	Nod2 nucleic acids and proteins
33	US 20020088015 A1	20020704	64	WILMS' TUMOR WT1 BINDING PROTEINS
34	US 20020082410 A1	20020627	34	Insulin promoter factor, and uses related thereto
35	US 20020082392 A1	20020627	62	ANTIBODIES TO CELL-CYCLE REGULATORY PROTEINS, AND USES RELATED THERETO

	Document ID	Issue Date	Pages	Title
36	US 20020045206 A1	20020418	77	VERTEBRATE EMBRYONIC PATTERNING-INDUCING PROTEINS, COMPOSITIONS AND USES RELATED THERTO
37	US 20020034758 A1	20020321	50	Novel human genes and gene expressions products: II
38	US 20020032323 A1	20020314	64	STREPTOCOCCUS PNEUMONIAE POLYNUCLEOTIDES AND SEQUENCES
39	US 20020025569 A1	20020228	44	COMPONENTS OF UBIQUITIN LIGASE COMPLEXES AND USES RELATED THERETO
40	US 20020025305 A1	20020228	54	CELL-CYCLE REGULATORY PROTEINS, AND USES RELATED THERETO
41	US 20010047078 A1	20011129	10	Methods for identifying inhibitors of methionine aminopeptidases
42	US 20010041353 A1	20011115	36	Novel SSP-1 compositions and therapeutic and diagnostic uses therefor
43	US 6593454 B2	20030715	11	Methods for identifying inhibitors of methionine aminopeptidases
44	US 6593104 B1	20030715	58	Macular degeneration diagnostics and therapeutics
45	US 6576237 B1	20030610	120	Vertebrate tissue pattern-inducing proteins, and uses related thereto
46	US 6573370 B1	20030603	73	PON3 and uses thereof
47	US 6518411 B1	20030211	101	RGS compositions and therapeutic and diagnostic uses therefor

	Document ID	Issue Date	Pages	Title
48	US 6514724 B1	20030204	69	Hedgehog interacting proteins and uses related thereto
49	US 6509152 B1	20030121	59	Immunosuppressant target proteins
50	US 6503742 B1	20030107	47	Ubiquitin ligases and uses related thereto
51	US 6486131 B2	20021126	54	Cell-cycle regulatory proteins, and uses related thereto
52	US 6479261 B1	20021112	288	Methods of using interleukin-3 (IL-3) mutant polypeptides for ex-vivo expansion of hematopoietic stem cells
53	US 6464974 B1	20021015	57	Immunosuppressant target proteins
54	US 6458931 B1	20021001	314	Interleukin-3 (IL-3) multiple mutation polypeptides
55	US 6436677 B1	20020820	54	Method of reverse transcription
56	US 6428977 B1	20020806	61	Signalin family of TGF.beta. signal transduction proteins, and uses related thereto
57	US 6403307 B1	20020611	68	Glaucoma therapeutics and diagnostics
58	US 6403076 B1	20020611	86	Compositions for increasing hematopoiesis with interleukin-3 mutants

	Document ID	Issue Date	Pages	Title
59	US 6399760 B1	20020604	53	RP compositions and therapeutic and diagnostic uses therefor
60	US 6399349 B1	20020604	120	Human aminopeptidase P gene
61	US 6399326 B1	20020604	51	Nucleic acids encoding neural/pancreatic receptor tyrosine phosphatase
62	US 6395526 B1	20020528	38	DNA polymerase
63	US 6384192 B1	20020507	118	Vertebrate embryonic pattern-inducing proteins
64	US 6379662 B1	20020430	112	Co-administration of interleukin-3 mutant polypeptides with CSF's for multi-lineage hematopoietic cell production
65	US 6361977 B1	20020326	264	Methods of using multivariant IL-3 hematopoiesis fusion protein
66	US 6361976 B1	20020326	130	Co-administration of interleukin-3 mutant polypeptides with CSF'S for multi-lineage hematopoietic cell production
67	US 6331390 B1	20011218	65	Cell-cycle regulatory proteins, and uses related thereto
68	US 6309879 B1	20011030	36	Human patched genes and proteins, and uses related thereto

	Document ID	Issue Date	Pages	Title
69	US 6306586 B1	20011023	62	Methods and compositions for the diagnosis and treatment of cataracts
70	US 6296853 B1	20011002	43	E6 binding proteins
71	US 6274342 B1	20010814	39	Nucleic acid molecules encoding monocyte chemotactic protein 5 (MCP-5) molecules and uses therefor
72	US 6271363 B1	20010807	119	Nucleic acids encoding hedgehog proteins
73	US 6271026 B1	20010807	45	Glaucoma compositions
74	US 6268476 B1	20010731	37	EPH receptor ligands, and uses related thereto
75	US 6262334 B1	20010717	259	Human genes and expression products: II
76	US 6262333 B1	20010717	381	Human genes and gene expression products

	Document ID	Issue Date	Pages	Title
77	US 6261794 B1	20010717	9	Methods for identifying inhibitors of methionine aminopeptidases
78	US 6261786 B1	20010717	128	Screening assays for hedgehog agonists and antagonists
79	US 6225456 B1	20010501	50	Ras suppressor SUR-5
80	US 6211334 B1	20010403	67	Cell-cycle regulatory proteins, and uses related thereto
81	US 6207450 B1	20010327	54	Glaucoma therapeutics and diagnostics based on a novel human transcription factor
82	US 6197945 B1	20010306	33	Insulin promoter factor, and uses related thereto
83	US 6194556 B1	20010227	77	Angiotensin converting enzyme homolog and therapeutic and diagnostic uses therfor
84	US 6171798 B1	20010109	32	P53-regulated genes
85	US 6165747 A	20001226	120	Nucleic acids encoding hedgehog proteins
86	US 6153183 A	20001128	131	Co-administration of interleukin-3 mutant polypeptides with CSF's or cytokines for multi-lineage hematopoietic cell production

	Document ID	Issue Date	Pages	Title
87	US 6150137 A	20001121	60	Immunosuppressant target proteins
88	US 6147192 A	20001114	48	Tub interactor (TI) polypeptides and uses therefor
89	US 6143491 A	20001107	46	Therapeutic compositions and methods and diagnostic assays for type II diabetes involving HNF-1
90	US 6132991 A	20001017	87	Human interleukin-3 (IL-3) variant fusion proteins
91	US 6130318 A	20001010	21	hIL-4 mutant proteins used as antagonists or partial agonists of human interleukin 4
92	US 6127521 A	20001003	60	Immunosuppressant target proteins
93	US 6127158 A	20001003	32	Ubiquitin conjugating enzymes
94	US 6121045 A	20000919	70	Human Delta3 nucleic acid molecules
95	US 6093395 A	20000725	141	Co-administration of interleukin-3 mutant polypeptides with CSF's for multi-lineage hematopoietic cell production
96	US 6087107 A	20000711	54	Therapeutics and diagnostics for congenital heart disease based on a novel human transcription factor
97	US 6074639 A	20000613	90	Ex vivo expansion of hematopoietic cells using interleukin-3 (IL-3) variant fusion proteins

	Document ID	Issue Date	Pages	Title
98	US 6068982 A	20000530	73	Ubiquitin conjugating enzymes
99	US 6066318 A	20000523	321	Multi-functional hematopoietic fusion proteins between sequence rearranged C-MPL receptor agonists and other hematopoietic factors
100	US 6060262 A	20000509	40	Regulation of I Kappa B (I.kappa.B) degradation and methods and reagents related thereto
101	US 6060047 A	20000509	122	Co-administration of interleukin-3 mutant polypeptides with CSF's for multi-lineage hematopoietic cell production
102	US 6057427 A	20000502	66	Antibody to cytokine response gene 2(CR2) polypeptide
103	US 6057133 A	20000502	113	Multivariant human IL-3 fusion proteins and their recombinant production

	Document ID	Issue Date	Pages	Title
104	US 6051398 A	20000418	71	Nucleic acids encoding CR3 polypeptide, vector and transformed cell thereof, and expression thereof
105	US 6046308 A	20000404	55	Isolated TRBP polypeptides and uses therefor
106	US 6043030 A	20000328	62	Cell-cycle regulatory proteins, and uses related thereto
107	US 6037173 A	20000314	55	Isolated nucleic acid encoding TRBP
108	US 6031076 A	20000229	43	Conservin compositions
109	US 6030812 A	20000229	257	Fusion proteins comprising multiply mutated interleukin-3 (IL-3) polypeptides and second growth factors
110	US 6027914 A	20000222	72	Nucleic acids encoding CR6 polypeptide vector and transformed cell thereof, and expression thereof
111	US 6022535 A	20000208	276	Treatment of hematopoietic disorders with fusion proteins comprising multiply mutated interleukin-3 (IL-3) polypeptides and second growth factors
112	US 6020155 A	20000201	72	Nucleic acids encoding CR1 fusion protein, vector, transfected cell and expression
113	US 6020135 A	20000201	33	P53-regulated genes

	Document ID	Issue Date	Pages	Title
114	US 6015692 A	20000118	32	CDC37 cell-cycle regulatory protein and uses related thereto
115	US 6008014 A	19991228	47	Method of making lipid metabolic pathway compositions
116	US 6001619 A	19991214	49	Ubiquitin ligases, and uses related thereto
117	US 5997860 A	19991207	79	Ex-vivo expansion of stem cells using combinations of interleukin-3 (IL-3) variants and other cytokines
118	US 5997857 A	19991207	114	Co-administration of interleukin-3 mutants with colony stimulating factors
119	US 5989804 A	19991123	42	E6 binding proteins
120	US 5981702 A	19991109	35	Cyclin/CDK associated proteins, and uses related thereto
121	US 5981699 A	19991109	85	Human ubiquitin conjugating enzyme
122	US 5968821 A	19991019	52	Cell-cycle regulatory proteins, and uses related thereto
123	US 5968761 A	19991019	61	Ubiquitin conjugating enzymes

	Document ID	Issue Date	Pages	Title
124	US 5962316 A	19991005	52	Cell-cycle regulatory proteins, and uses related thereto
125	US 5955306 A	19990921	64	Genes encoding proteins that interact with the tub protein
126	US 5912326 A	19990615	38	Cerebellum-derived growth factors
127	US 5912141 A	19990615	41	Nucleic acids encoding tumor virus susceptibility genes
128	US 5889169 A	19990330	32	Cell cycle regulatory protein p16 gene
129	US 5885776 A	19990323	43	Glaucoma compositions and therapeutic and diagnositic uses therefor
130	US 5882894 A	19990316	69	Nucleic acids encoding CR8 polypeptides, vector and transformed cell thereof, and expression thereof
131	US 5871961 A	19990216	72	Nucleic acids encoding CR2 polypeptides, vector and transformed cell thereof, and expression thereof
132	US 5871960 A	19990216	73	Nucleic acids encoding CR5 polypeptide, vector and transformed cell thereof, and expression thereof

	Document ID	Issue Date	Pages	Title
133	US 5849989 A	19981215	33	Insulin promoter factor, and uses related thereto
134	US 5844079 A	19981201	111	Vertebrate embryonic pattern-inducing proteins, and uses related thereto
135	US 5821051 A	19981013	33	E6 binding proteins
136	US 5807708 A	19980915	42	Conservin nucleic acid molecules and compositions
137	US 5800998 A	19980901	36	Assays for diagnosing type II diabetes in a subject
138	US 5795734 A	19980818	53	EPH receptor ligands, and uses related thereto
139	US 5795726 A	19980818	47	Methods for identifying compounds useful in treating type II diabetes
140	US 5792833 A	19980811	48	E2 binding proteins
141	US 5772992 A	19980630	89	Compositions for co-administration of interleukin-3 mutants and other cytokines and hematopoietic factors
142	US 5770384 A	19980623	49	Method for determining compound interaction with E2 binding proteins
143	US 5756671 A	19980526	32	CDC37 cell-cycle regulatory protein, and uses related thereto

	Document ID	Issue Date	Pages	Title
144	US 5744343 A	19980428	75	Ubiquitin conjugating enzymes
145	US 5738849 A	19980414	87	Interleukin-3 (IL-3) variant fusion proteins, their recombinant production, and therapeutic compositions comprising them
146	US 5691147 A	19971125	62	CDK4 binding assay
147	US 5136023 A	19920804	8	Polypeptide with cell-spreading activity

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11 FILES IN THE FILE LIST

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FILE 'EMBASE'
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L34          16 L22 NOT 2001-2003/PY

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=> dup rem l36
PROCESSING COMPLETED FOR L36
L37          64 DUP REM L36 (108 DUPLICATES REMOVED)

=> d tot

L37  ANSWER 1 OF 64  SCISEARCH  COPYRIGHT 2003 THOMSON ISI on STN
TI   Identification of critical residues in the active site of porcine
     membrane-bound aminopeptidase P
SO   BIOCHEMISTRY, (12 DEC 2000) Vol. 39, No. 49, pp. 15129-15135.
     Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
```

ISSN: 0006-2960.
AU Cottrell G S; Hyde R J; Lim J; Parsons M R; Hooper N M; Turner A J (Reprint)
AN 2001:1352 SCISEARCH

L37 ANSWER 2 OF 64 MEDLINE on STN DUPLICATE 1
TI cis-fumagillin, a new **methionine aminopeptidase** (type 2) inhibitor produced by Penicillium sp. F2757.
SO JOURNAL OF ANTIBIOTICS, (2000 Aug) 53 (8) 799-806.
Journal code: 0151115. ISSN: 0021-8820.
AU Kwon J Y; Jeong H W; Kim H K; Kang K H; Chang Y H; Bae K S; Choi J D; Lee U C; Son K H; Kwon B M
AN 2001056253 MEDLINE

L37 ANSWER 3 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI The biochemical and molecular characterization of recombinant Bacillus subtilis tripeptidase (PepT) as a zinc-dependent metalloenzyme
SO MOLECULES AND CELLS, (31 AUG 2000) Vol. 10, No. 4, pp. 423-431.
Publisher: SPRINGER-VERLAG SINGAPORE PTE LTD, #04-01 CENCON I, 1 TANNERY RD, SINGAPORE 347719, SINGAPORE.
ISSN: 1016-8478.
AU Cha M H; Yong W M; Lee S M; Lee Y S; Chung I Y (Reprint)
AN 2000:659706 SCISEARCH

L37 ANSWER 4 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
TI Structural Determinants of Post-translational Modification and Catalytic Specificity for the Lipoyl Domains of the Pyruvate Dehydrogenase Multienzyme Complex of Escherichia coli
SO Journal of Molecular Biology (2000), 295(2), 289-306
CODEN: JMOBAK; ISSN: 0022-2836
AU Jones, D. Dafydd; Horne, H. James; Reche, Pedro A.; Perham, Richard N.
AN 2000:12471 HCAPLUS
DN 132:204777

L37 ANSWER 5 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
TI Novel effects of a transposon insertion in the Vibrio fischeri glnD gene: defects in iron uptake and symbiotic persistence in addition to nitrogen utilization
SO Molecular Microbiology (2000), 37(1), 168-179
CODEN: MOMIEE; ISSN: 0950-382X
AU Graf, J.; Ruby, E. G.
AN 2000:557742 HCAPLUS
DN 134:37708

L37 ANSWER 6 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI Cloning, chromosomal sublocalization of the human soluble aminopeptidase P gene (XPNPEP1) to 10q25.3 and conservation of the putative proton shuttle and metal ligand binding sites with XPNPEP2
SO ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1 JUN 2000) Vol. 378, No. 1, pp. 51-56.
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 0003-9861.
AU Sprinkle T J (Reprint); Caldwell C; Ryan J W
AN 2000:456938 SCISEARCH

L37 ANSWER 7 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI The action of N-terminal acetyltransferases on yeast ribosomal proteins
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (24 DEC 1999) Vol. 274, No. 52, pp. 37035-37040.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0021-9258.
AU Arnold R J; Polevoda B; Reilly J P; Sherman F (Reprint)

AN 2000:11986 SCISEARCH

L37 ANSWER 8 OF 64 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN DUPLICATE 2
TI Erratum: Yeast **methionine aminopeptidase** I. Alteration of substrate specificity by site-directed **mutagenesis** (Journal of Biological Chemistry (1999) 274 (13403-13409)).
SO Journal of Biological Chemistry, (17 Sep 1999) 274/38 (27338). ISSN: 0021-9258 CODEN: JBCHA3
AU Walker K.W.; Bradshaw R.A.
AN 1999326765 EMBASE

L37 ANSWER 9 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI Yeast **methionine aminopeptidase** I. Alteration of substrate specificity by site-directed **mutagenesis**. (vol 274, pg 13403, 1999)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (17 SEP 1999) Vol. 274, No. 38, pp. 27338-27338.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0021-9258.
AU Walker K W (Reprint); Bradshaw R A
AN 1999:719930 SCISEARCH

L37 ANSWER 10 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
TI Yeast **methionine aminopeptidase** I. Alteration of substrate specificity by site-directed **mutagenesis**. [Erratum to document cited in CA131:113089]
SO Journal of Biological Chemistry (1999), 274(38), 27338 CODEN: JBCHA3; ISSN: 0021-9258
AU Walker, Kenneth W.; Bradshaw, Ralph A.
AN 1999:622783 HCAPLUS
DN 131:334040

L37 ANSWER 11 OF 64 MEDLINE on STN DUPLICATE 3
TI Yeast **methionine aminopeptidase** I. Alteration of substrate specificity by site-directed **mutagenesis**.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 May 7) 274 (19) 13403-9. Journal code: 2985121R. ISSN: 0021-9258.
AU Walker K W; Bradshaw R A
AN 1999240731 MEDLINE

L37 ANSWER 12 OF 64 MEDLINE on STN DUPLICATE 4
TI Escherichia coli **methionine aminopeptidase**: implications of crystallographic analyses of the native, **mutant**, and inhibited enzymes for the mechanism of catalysis.
SO BIOCHEMISTRY, (1999 Jun 15) 38 (24) 7678-88. Journal code: 0370623. ISSN: 0006-2960.
AU Lowther W T; Orville A M; Madden D T; Lim S; Rich D H; Matthews B W
AN 1999316170 MEDLINE

L37 ANSWER 13 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI Identification and specificities of N-terminal acetyltransferases from Saccharomyces cerevisiae
SO EMBO JOURNAL, (1 NOV 1999) Vol. 18, No. 21, pp. 6155-6168.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 0261-4189.
AU Polevoda B; Norbeck J; Takakura H; Blomberg A; Sherman F (Reprint)
AN 1999:882809 SCISEARCH

L37 ANSWER 14 OF 64 MEDLINE on STN DUPLICATE 5
TI Amino acid residues involved in the functional integrity of Escherichia coli **methionine aminopeptidase**.
SO JOURNAL OF BACTERIOLOGY, (1999 Aug) 181 (15) 4686-9.

Journal code: 2985120R. ISSN: 0021-9193.
AU Chiu C H; Lee C Z; Lin K S; Tam M F; Lin L Y
AN 1999350439 MEDLINE

L37 ANSWER 15 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI Eukaryotic 20S proteasome catalytic subunit propeptides prevent active site inactivation by N-terminal acetylation and promote particle assembly
SO EMBO JOURNAL, (1 JUL 1999) Vol. 18, No. 13, pp. 3575-3585.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 0261-4189.
AU Arendt C S; Hochstrasser M (Reprint)
AN 1999:571918 SCISEARCH

L37 ANSWER 16 OF 64 MEDLINE on STN DUPLICATE 6
TI The loss in hydrophobic surface area resulting from a Leu to Val **mutation** at the N-terminus of the aldehyde dehydrogenase presequence prevents import of the protein into mitochondria.
SO PROTEIN SCIENCE, (1999 Apr) 8 (4) 890-6.
Journal code: 9211750. ISSN: 0961-8368.
AU Hammen P K; Heard T S; Waltner M; Weiner H
AN 1999226817 MEDLINE

L37 ANSWER 17 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI Effect of foreign N-terminal residues on the conformational stability of human lysozyme
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (DEC 1999) Vol. 266, No. 2, pp. 675-682.
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0014-2956.
AU Takano K; Tsuchimori K; Yamagata Y; Yutani K (Reprint)
AN 2000:17818 SCISEARCH

L37 ANSWER 18 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI Characterization of a prolidase from Lactobacillus delbrueckii subsp. bulgaricus CNRZ 397 with an unusual regulation of biosynthesis
SO MICROBIOLOGY-UK, (FEB 1999) Vol. 145, Part 2, pp. 437-446.
Publisher: SOC GENERAL MICROBIOLOGY, MARLBOROUGH HOUSE, BASINGSTOKE RD, SPENCERS WOODS, READING RG7 1AE, BERKS, ENGLAND.
ISSN: 1350-0872.
AU Morel F; FrotCoutaz J; Aubel D; Portalier R; Atlan D (Reprint)
AN 1999:160285 SCISEARCH

L37 ANSWER 19 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI The purification and characterization of Bacillus subtilis tripeptidase (PepT)
SO JOURNAL OF BIOCHEMISTRY AND MOLECULAR BIOLOGY, (31 MAY 1999) Vol. 32, No. 3, pp. 239-246.
Publisher: SPRINGER-VERLAG SINGAPORE PTE LTD, #04-01 CENCON I, 1 TANNERY RD, SINGAPORE 347719, SINGAPORE.
ISSN: 1225-8687.
AU Park Y S; Cha M H; Yong W M; Kim H J; Chung I Y (Reprint); Lee Y S
AN 1999:418714 SCISEARCH

L37 ANSWER 20 OF 64 MEDLINE on STN DUPLICATE 7
TI Production of "authentic" poliovirus RNA-dependent RNA polymerase (3D(pol)) by ubiquitin-protease-mediated cleavage in Escherichia coli.
SO PROTEIN EXPRESSION AND PURIFICATION, (1999 Oct) 17 (1) 128-38.
Journal code: 9101496. ISSN: 1046-5928.
AU Gohara D W; Ha C S; Kumar S; Ghosh B; Arnold J J; Wisniewski T J; Cameron C E
AN 1999428399 MEDLINE

L37 ANSWER 21 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI Generation of S. cerevisiae **mutants** resistant to the

angiogenesis inhibitor fumagillin.
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 126.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research
. ISSN: 0197-016X.
AU Eng, W.-K.; Faucette, L. F.; Raup, J. L.; Johnson, R. K.
AN 1999:216969 BIOSIS

L37 ANSWER 22 OF 64 MEDLINE on STN DUPLICATE 8
TI A **methionine aminopeptidase** and putative regulator of translation initiation is required for cell growth and patterning in Drosophila.
SO MECHANISMS OF DEVELOPMENT, (1999 Apr) 82 (1-2) 23-8.
Journal code: 9101218. ISSN: 0925-4773.
AU Cutforth T; Gaul U
AN 1999284515 MEDLINE

L37 ANSWER 23 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI An Escherichia coli expression vector that allows recovery of proteins with native N-termini from purified calmodulin-binding peptide fusions
SO PROTEIN EXPRESSION AND PURIFICATION, (JUN 1999) Vol. 16, No. 1, pp. 1-10.
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 1046-5928.
AU Wyborski D L; Bauer J C; Zheng C F; Felts K; Vaillancourt P (Reprint)
AN 1999:426446 SCISEARCH

L37 ANSWER 24 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
TI Cloning and expression of genes for unmodified recombinant human adult hemoglobin production
SO U.S., 21 pp.
CODEN: USXXAM
IN Ho, Chien; Shen, Tong-jian
AN 1998:324789 HCAPLUS
DN 129:1443

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5753465	A	19980519	US 1994-298339	19940830

L37 ANSWER 25 OF 64 MEDLINE on STN DUPLICATE 9
TI Molecular recognition of angiogenesis inhibitors fumagillin and ovalicin by **methionine aminopeptidase** 2.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Dec 22) 95 (26) 15183-8.
Journal code: 7505876. ISSN: 0027-8424.
AU Griffith E C; Su Z; Niwayama S; Ramsay C A; Chang Y H; Liu J O
AN 1999079987 MEDLINE

L37 ANSWER 26 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
TI '98 Escherichia coli SWISS-2DPAGE database update
SO Electrophoresis (1998), 19(11), 1960-1971
CODEN: ELCTDN; ISSN: 0173-0835
AU Tonella, Luisa; Walsh, Brad J.; Sanchez, Jean-Charles; Ou, Keli; Wilkins, Marc R.; Tyler, Margaret; Frutiger, Severine; Gooley, Andrew A.; Pescaru, Ioana; Appel, Ron D.; Yan, Jun X.; Bairoch, Amos; Hoogland, Christine; Morch, Fabienne S.; Hughes, Graham J.; Williams, Keith L.; Hochstrasser, Denis F.
AN 1998:635865 HCAPLUS
DN 129:299940

L37 ANSWER 27 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI Spectroscopic identification of a dinuclear metal centre in

manganese(II)-activated aminopeptidase P from Escherichia coli: implications for human prolidase
SO JOURNAL OF BIOLOGICAL INORGANIC CHEMISTRY, (OCT 1998) Vol. 3, No. 5, pp. 470-483.
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010.
ISSN: 0949-8257.
AU Zhang L B; Crossley M J; Dixon N E; Ellis P J; Fisher M L; King G F; Lilley P E; MacLachlan D; Pace R J; Freeman H C (Reprint)
AN 1998:830774 SCISEARCH

L37 ANSWER 28 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI Recognition of AUG and alternative initiator codons is augmented by G in position +4 but is not generally affected by the nucleotides in positions +5 and +6
SO EMBO JOURNAL, (1 MAY 1997) Vol. 16, No. 9, pp. 2482-2492.
Publisher: OXFORD UNIV PRESS, WALTON ST JOURNALS DEPT, OXFORD, ENGLAND OX2 6DP.
ISSN: 0261-4189.
AU Kozak M (Reprint)
AN 97:384586 SCISEARCH

L37 ANSWER 29 OF 64 MEDLINE on STN DUPLICATE 10
TI Improvement of the refolding yield and solubility of hen egg-white lysozyme by altering the Met residue attached to its N-terminus to Ser.
SO PROTEIN ENGINEERING, (1997 Nov) 10 (11) 1333-8.
Journal code: 8801484. ISSN: 0269-2139.
AU Mine S; Ueda T; Hashimoto Y; Imoto T
AN 1998173056 MEDLINE

L37 ANSWER 30 OF 64 Elsevier BIOBASE COPYRIGHT 2003 Elsevier Science B.V. on STN
AN 1997246025 ESBIOBASE
TI **Methionine aminopeptidase** from the hyperthermophilic archaeon pyrococcus furiosus: Molecular cloning and overexperssion in Escherichia coli of the gene, and characteristics of the enzyme
AU Tsunasawa S.; Izu Y.; Miyagi M.; Kato I.
CS S. Tsunasawa, Biotechnology Research Laboratories, Takara Shuzo Co. Ltd., Kusatsu, Shiga 525, Japan.
E-mail: s-tsunas@mx.biwa.or.jp
SO Journal of Biochemistry, (1997), 122/4 (843-850), 24 reference(s)
CODEN: JOBIAO ISSN: 0021-924X
DT Journal; Article
CY Japan
LA English
SL English

L37 ANSWER 31 OF 64 MEDLINE on STN DUPLICATE 11
TI A dominant negative **mutation** in Saccharomyces cerevisiae **methionine aminopeptidase**-1 affects catalysis and interferes with the function of **methionine aminopeptidase**-2.
SO ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1997 Nov 15) 347 (2) 193-200.
Journal code: 0372430. ISSN: 0003-9861.
AU Klinkenberg M; Ling C; Chang Y H
AN 1998035818 MEDLINE

L37 ANSWER 32 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI CDC48P INTERACTS WITH UFD3P, A WD REPEAT PROTEIN REQUIRED FOR UBIQUITIN-MEDIATED PROTEOLYSIS IN SACCHAROMYCES-CEREVISIAE
SO EMBO JOURNAL, (16 SEP 1996) Vol. 15, No. 18, pp. 4884-4899.
ISSN: 0261-4189.
AU GHISLAIN M; DOHMEN R J; LEVY F; VARSHAVSKY A (Reprint)
AN 96:732219 SCISEARCH

L37 ANSWER 33 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN DUPLICATE 12
TI SURFACE LOCATION OF HPR, A PHOSPHOCARRIER OF THE PHOSPHOENOLPYRUVATE-SUGAR PHOSPHOTRANSFERASE SYSTEM IN STREPTOCOCCUS-SUIS
SO MICROBIOLOGY-UK, (APR 1996) Vol. 142, Part 4, pp. 837-843.
ISSN: 1350-0872.
AU DUBREUIL J D; JACQUES M; BROCHU D; FRENETTE M; VADEBONCOEUR C (Reprint)
AN 96:349520 SCISEARCH

L37 ANSWER 34 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI ISOLATION AND CHARACTERIZATION OF RECOMBINANT HUMAN APOLIPOPROTEIN C-II EXPRESSED IN ESCHERICHIA-COLI
SO BIOCHIMICA ET BIOPHYSICA ACTA-LIPIDS AND LIPID METABOLISM, (16 AUG 1996) Vol. 1302, No. 3, pp. 224-230.
ISSN: 0005-2760.
AU WANG C S (Reprint); DOWNS D; DASHTI A; JACKSON K W
AN 96:632367 SCISEARCH

L37 ANSWER 35 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI AMINO-TERMINAL PROTEIN PROCESSING IN SACCHAROMYCES-CEREVISIAE IS AN ESSENTIAL FUNCTION THAT REQUIRES 2 DISTINCT **METHIONINE AMINOPEPTIDASES**
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (19 DEC 1995) Vol. 92, No. 26, pp. 12357-12361.
ISSN: 0027-8424.
AU LI X (Reprint); CHANG Y H
AN 96:27590 SCISEARCH

L37 ANSWER 36 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI SYNTHETIC SIGNALS FOR UBIQUITIN-DEPENDENT PROTEOLYSIS
SO MOLECULAR AND CELLULAR BIOLOGY, (AUG 1995) Vol. 15, No. 8, pp. 4086-4094.
ISSN: 0270-7306.
AU SADIS S; ATIENZA C; FINLEY D (Reprint)
AN 95:498150 SCISEARCH

L37 ANSWER 37 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
TI Recombinant protein sequences can trigger methylation of N-terminal amino acids in Escherichia coli
SO Protein Science (1995), 4(12), 2616-18
CODEN: PRCIEI; ISSN: 0961-8368
AU Apostol, izydor; Aitken, Jackie; Levine, Joe; Lippcott, Julie; Davidson, Jeffrey S.; Abbott-Brown, Debbie
AN 1995:977454 HCAPLUS
DN 124:25340

L37 ANSWER 38 OF 64 MEDLINE on STN DUPLICATE 13
TI A novel low oxygen affinity recombinant hemoglobin (alpha96val--> Trp): switching quaternary structure without changing the ligation state.
SO JOURNAL OF MOLECULAR BIOLOGY, (1995 May 12) 248 (4) 867-82.
Journal code: 2985088R. ISSN: 0022-2836.
AU Kim H W; Shen T J; Sun D P; Ho N T; Madrid M; Ho C
AN 95271672 MEDLINE

L37 ANSWER 39 OF 64 MEDLINE on STN DUPLICATE 14
TI Evidence that two zinc fingers in the **methionine aminopeptidase** from Saccharomyces cerevisiae are important for normal growth.
SO MOLECULAR AND GENERAL GENETICS, (1995 Jan 20) 246 (2) 247-53.
Journal code: 0125036. ISSN: 0026-8925.
AU Zuo S; Guo Q; Ling C; Chang Y H
AN 95166182 MEDLINE

L37 ANSWER 40 OF 64 MEDLINE on STN DUPLICATE 15
TI The role of nucleotides conserved in eukaryotic initiator methionine tRNAs in initiation of protein synthesis.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Nov 25) 268 (33) 25221-8.
Journal code: 2985121R. ISSN: 0021-9258.
AU Drabkin H J; Helk B; RajBhandary U L
AN 94043395 MEDLINE

L37 ANSWER 41 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI GLUTAMINE INHIBITS THE AMMONIA-DEPENDENT ACTIVITIES OF 2 CYS-1 **MUTANTS** OF HUMAN ASPARAGINE SYNTHETASE THROUGH THE FORMATION OF AN ABORTIVE COMPLEX
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (05 AUG 1993) Vol. 268, No. 22, pp. 16771-16780.
ISSN: 0021-9258.
AU SHENG S; MORAGAAMADOR D A; VANHEEKE G; ALLISON R D; RICHARDS N G J; SCHUSTER S M (Reprint)
AN 93:482003 SCISEARCH

L37 ANSWER 42 OF 64 MEDLINE on STN
TI Human immunodeficiency virus reverse transcriptase. Expression in Escherichia coli, purification, and characterization of a functionally and structurally asymmetric dimeric polymerase.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Aug 5) 268 (22) 16528-36.
Journal code: 2985121R. ISSN: 0021-9258.
AU Thimmig R L; McHenry C S
AN 93346401 MEDLINE

L37 ANSWER 43 OF 64 MEDLINE on STN DUPLICATE 16
TI Production of unmodified human adult hemoglobin in Escherichia coli.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1993 Sep 1) 90 (17) 8108-12.
Journal code: 7505876. ISSN: 0027-8424.
AU Shen T J; Ho N T; Simplaceanu V; Zou M; Green B N; Tam M F; Ho C
AN 93376752 MEDLINE

L37 ANSWER 44 OF 64 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
TI Production of unmodified human adult hemoglobin in Escherichia coli; using plasmid pHE2 in which the alpha-globin and beta-globin genes are coexpressed with **methionine-aminopeptidase**
SO Proc.Natl.Acad.Sci.U.S.A.; (1993) 90, 17, 8108-12
CODEN: PNASA6
AU Shen J T; Ho N T; Simplaceanu V; Zou M; Green B N; *Ho C
AN 1993-12043 BIOTECHDS

L37 ANSWER 45 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI YEAST MAK3 N-ACETYLTRANSFERASE RECOGNIZES THE N-TERMINAL 4 AMINO-ACIDS OF THE MAJOR COAT PROTEIN (GAG) OF THE L-A DOUBLE-STRANDED-RNA VIRUS
SO JOURNAL OF BACTERIOLOGY, (MAY 1993) Vol. 175, No. 10, pp. 3192-3194.
ISSN: 0021-9193.
AU TERCERO J C; DINMAN J D; WICKNER R B (Reprint)
AN 93:320592 SCISEARCH

L37 ANSWER 46 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI Yeast **methionine aminopeptidase** contains two zinc fingers and one cobalt-dependent catalytic domain.
SO FASEB Journal, (1993) Vol. 7, No. 7, pp. A1181.
Meeting Info.: Joint Meeting of the American Society for Biochemistry and Molecular Biology and American Chemical Society Division of Biological Chemistry San Diego, California, USA May 30-June 3, 1993
ISSN: 0892-6638.
AU Chang, Y.-H.; Zuo, S. L.
AN 1993:336067 BIOSIS

L37 ANSWER 47 OF 64 MEDLINE on STN DUPLICATE 17
TI Isolation and characterization of the **methionine aminopeptidase** from porcine liver responsible for the

co-translational processing of proteins.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Oct 15) 267 (29) 20667-73.
Journal code: 2985121R. ISSN: 0021-9258.
AU Kendall R L; Bradshaw R A
AN 93015964 MEDLINE

L37 ANSWER 48 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
TI Molecular cloning, sequencing, deletion, and overexpression of a **methionine aminopeptidase** gene from Saccharomyces cerevisiae
SO Journal of Biological Chemistry (1992), 267(12), 8007-11
CODEN: JBCHA3; ISSN: 0021-9258
AU Chang, Yie Hwa; Teichert, Ulrich; Smith, John A.
AN 1992:422435 HCAPLUS
DN 117:22435

L37 ANSWER 49 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI PARAMETERS AFFECTING THE FREQUENCIES OF TRANSFORMATION AND COTRANSFORMATION WITH SYNTHETIC OLIGONUCLEOTIDES IN YEAST
SO YEAST, (NOV 1992) Vol. 8, No. 11, pp. 935-948.
ISSN: 0749-503X.
AU YAMAMOTO T; MOERSCHELL R P; WAKEM L P; FERGUSON D; SHERMAN F (Reprint)
AN 92:700755 SCISEARCH

L37 ANSWER 50 OF 64 MEDLINE on STN DUPLICATE 18
TI Expression of a group II phospholipase A2 from the venom of Agkistrodon piscivorus piscivorus in Escherichia coli: recovery and renaturation from bacterial inclusion bodies.
SO PROTEIN EXPRESSION AND PURIFICATION, (1992 Dec) 3 (6) 512-7.
Journal code: 9101496. ISSN: 1046-5928.
AU Lathrop B K; Burack W R; Biltonen R L; Rule G S
AN 93136711 MEDLINE

L37 ANSWER 51 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI DOES UNCONTROLLED SURVIVAL OF ACETYLATED PEPTIDES LEAD TO CELL-PROLIFERATION - DELETION OF N-TERMINAL DEACETYLATING SYSTEM FOR PROTEIN PEPTIDE IN SMALL-CELL LUNG-CARCINOMA CELLS
SO JOURNAL OF LABORATORY AND CLINICAL MEDICINE, (OCT 1992) Vol. 120, No. 4, pp. 505-506.
ISSN: 0022-2143.
AU TSUNASAWA S (Reprint)
AN 92:635176 SCISEARCH

L37 ANSWER 52 OF 64 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
TI The use of genetic engineering methods to improve fermentation processes; strain improvement for reduced fermentation costs (conference paper)
SO Biol.Recombinant Microorg.Anim.Cells; (1991) Oholo 34 Meet., 17-31
AU Ben-Bassat A
AN 1992-06073 BIOTECHDS

L37 ANSWER 53 OF 64 LIFESCI COPYRIGHT 2003 CSA on STN
TI Cloning and nucleotide sequence of the Salmonella typhimurium pepM gene.
SO MOL. GEN. GENET., (1990) vol. 223, no. 2, pp. 345-348.
AU Movva, N.R.; Semon, D.; Meyer, C.; Kawashima, E.; Wingfield, P.; Miller, J.L.; Miller, S.G.
AN 90:78693 LIFESCI

L37 ANSWER 54 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
TI Cloning and nucleotide sequence of the Salmonella typhimurium pepM gene
SO Molecular and General Genetics (1990), 223(2), 245-8
CODEN: MGGEAE; ISSN: 0026-8925
AU Movva, N. Rao; Semon, Dominique; Meyer, Christina; Kawashima, Eric; Wingfield, Paul; Miller, Judith L.; Miller, Charles G.
AN 1991:75950 HCAPLUS

DN 114:75950

L37 ANSWER 55 OF 64 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
TI Recombinant HIV virus proteins;
used in assays for detecting antibody against HIV virus, and incorporated into vaccine compositions
AN 1989-07469 BIOTECHDS
PI EP 311228 12 Apr 1989

L37 ANSWER 56 OF 64 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
TI Alteration of amino-terminal codons of human granulocyte colony stimulating factor increases expression levels and allows efficient processing by **methionine-aminopeptidase** in Escherichia coli;
gene cloning and site-directed **mutagenesis**
SO Gene; (1988) 65, 1, 13-22
CODEN: GENED6
AU Devlin P E; Drummond R J; Toy P; Mark D F; Watt K W K; Devlin J J
AN 1989-01919 BIOTECHDS

L37 ANSWER 57 OF 64 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
TI Cloning E. coli genes by oligonucleotide hybridization;
Escherichia coli
SO Nucleic Acids Res.; (1987) 15, 24, 10593-94
CODEN: NARHAD
AU Mayaux J F; Soubrier F; Latta M
AN 1988-01645 BIOTECHDS

L37 ANSWER 58 OF 64 MEDLINE on STN DUPLICATE 21
TI Specificity of cotranslational amino-terminal processing of proteins in yeast.
SO BIOCHEMISTRY, (1987 Dec 15) 26 (25) 8242-6.
Journal code: 0370623. ISSN: 0006-2960.
AU Huang S; Elliott R C; Liu P S; Koduri R K; Weickmann J L; Lee J H; Blair L C; Ghosh-Dastidar P; Bradshaw R A; Bryan K M; +
AN 88163485 MEDLINE

L37 ANSWER 59 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
TI N-terminal methionine-specific peptidase in Salmonella typhimurium
SO Proceedings of the National Academy of Sciences of the United States of America (1987), 84(9), 2718-22
CODEN: PNASA6; ISSN: 0027-8424
AU Miller, Charles G.; Strauch, Kathryn L.; Kukral, Anne M.; Miller, Judith L.; Wingfield, Paul T.; Mazzei, Gonzalo J.; Werlen, Raymond C.; Graber, Pierre; Movva, N. Rao
AN 1987:529597 HCAPLUS
DN 107:129597

L37 ANSWER 60 OF 64 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
TI Methionyl-aminopeptidase: processing of the initiator methionine of Escherichia coli proteins;
(conference abstract)
SO Protein Eng.; (1987) 1, 3, 265
CODEN: PRENE9
AU Hirel P H; Schmitter J M; Dessen P; Fayat G; Blanquet S
AN 1987-12132 BIOTECHDS

L37 ANSWER 61 OF 64 MEDLINE on STN DUPLICATE 22
TI Amino-terminal processing of **mutant** forms of yeast iso-1-cytochrome c. The specificities of **methionine aminopeptidase** and acetyltransferase.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1985 May 10) 260 (9) 5382-91.
Journal code: 2985121R. ISSN: 0021-9258.
AU Tsunasawa S; Stewart J W; Sherman F

AN 85182681 MEDLINE

L37 ANSWER 62 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
TI AMINO-TERMINAL PROCESSING OF **MUTANT** FORMS OF YEAST ISO-1-CYTOCHROME-C - THE SPECIFICITIES OF **METHIONINE AMINOPEPTIDASE** AND ACETYLTRANSFERASE
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1985) Vol. 260, No. 9, pp. 5382-5391.
AU TSUNASAWA S (Reprint); STEWART J W; SHERMAN F
AN 85:257406 SCISEARCH

L37 ANSWER 63 OF 64 MEDLINE on STN DUPLICATE 23
TI Characterization of human interleukin 2 derived from Escherichia coli.
SO BIOCHEMICAL JOURNAL, (1985 Jul 15) 229 (2) 429-39.
Journal code: 2984726R. ISSN: 0264-6021.
AU Liang S M; Allet B; Rose K; Hirschi M; Liang C M; Thatcher D R
AN 85306901 MEDLINE

L37 ANSWER 64 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
TI Identification and **mutational** relocation of the AUG codon initiating translation of iso-1-cytochrome c in yeast
SO Journal of Biological Chemistry (1971), 246(24), 7429-45
CODEN: JBCHA3; ISSN: 0021-9258
AU Stewart, John W.; Sherman, Fred; Shipman, Nancy A.; Jackson, Mary
AN 1972:11934 HCAPLUS
DN 76:11934

=> d ab 11,23, 24

L37 ANSWER 11 OF 64 MEDLINE on STN DUPLICATE 3
AB In eukaryotes, two isozymes (I and II) of **methionine aminopeptidase** (MetAP) catalyze the removal of the initiator methionine if the penultimate residue has a small radius of gyration (glycine, alanine, serine, threonine, proline, valine, and cysteine). Using site-directed **mutagenesis**, recombinant yeast MetAP I derivatives that are able to cleave N-terminal methionine from substrates that have larger penultimate residues have been expressed. A Met to Ala change at 329 (Met206 in Escherichia coli enzyme) produces an average catalytic efficiency 1.5-fold higher than the native enzyme on normal substrates and cleaves substrates containing penultimate asparagine, glutamine, isoleucine, leucine, methionine, and phenylalanine. Interestingly, the native enzyme also has significant activity with the asparagine peptide not previously identified as a substrate. **Mutation** of Gln356 (Gln233 in E. coli MetAP) to alanine results in a catalytic efficiency about one-third that of native with normal substrates but which can cleave methionine from substrates with penultimate histidine, asparagine, glutamine, leucine, methionine, phenylalanine, and tryptophan. **Mutation** of Ser195 to alanine had no effect on substrate specificity. None of the altered enzymes produced cleaved substrates with a fully charged residue (lysine, arginine, aspartic acid, or glutamic acid) or tyrosine in the penultimate position.

L37 ANSWER 23 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB We describe a T7-based Escherichia coli expression vector in which protein coding sequence is seamlessly fused to the N-terminal calmodulin-binding peptide (CBP) purification tag. We combined the use of the site-specific protease enterokinase (EK) and the type IIs restriction enzyme Eam1104 I, which cleave outside their respective (amino acid and nucleotide) target sequences, such that any amino acid sequence may be fused directly C-terminal to the EK cleavage site without codon constraints conferred by the cloning method. PCR products are cloned using ligation-dependent or ligation-independent methods with high cloning efficiencies (>10(6) cfu/mu g vector), allowing production of insert

quantities sufficient for several cloning experiments with a limited number of PCR cycles, resulting in a significant time-savings and reduced likelihood of accumulating PCR-derived **mutations**. CBP fusion proteins are expressed to high levels when the CBP peptide is positioned at the N-terminus. CBP binds to calmodulin with nanomolar affinity, and fusion proteins are purified to near homogeneity from crude extracts with one pass through calmodulin affinity resin using gentle binding and elution conditions. We show high efficiency seamless cloning of three inserts into the pCAL-n-EK vector, including one encoding the protein c-Jun N-terminal kinase (JNK). CBP-EK-JNK fusion protein was synthesized to 10-20 mg/liter culture and purified to near homogeneity in one step wit calmodulin affinity resin. The fusion tag was efficiently removed wit EK to yield active JNK wit native N-terminal amino acid sequence. (C) 1999 Academic Press.

L37 ANSWER 24 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN

AB Methods for obtaining unmodified recombinant human normal adult Hb A (rHb A) involve a novel expression plasmid that coexpressessu human .alpha.- and .beta.-globin genes and Escherichia coli **methionine aminopeptidase** genes under the control of sep. tac promoters. Methods are also provided for correcting an abnormal conformation of some of the heme groups incorporated in the proteins expressed by the expression plasmid. **Methionine aminopeptidase** cleaves the N-terminal methionines on the Hb A so that the mol. that is produced does not contain N-terminal methionines. The rHb A can be used as a component of a blood substitute or therapeutic agent, and the expression system can produced rHb A in high yield and also can be modified to produce **mutant** Hbs that are desired for therapeutic uses. Expression vector pHE2 which is used to express rHb A in E. coli is also claimed.

=> d ab 30, 34, 42, 43

L37 ANSWER 30 OF 64 Elsevier BIOBASE COPYRIGHT 2003 Elsevier Science B.V. on STN

AB A gene for a **methionine aminopeptidase** (MAP; EC 3.4.11.18), which catalyzes the removal of amino-terminal methionine from the growing peptide chain on the ribosome, has been cloned from the hyperthermophilic Archaeon, Pyrococcus furiosus, by a novel method effectively using its cosmid protein library, sequenced and expressed in Escherichia coli. The DNA sequence encodes a protein containing 295 amino acid residues with methionine at the N-terminus. From protein analyses of the recombinant protein expressed in E. coli, by using both amino acid sequence analysis from the N-terminus by automated Edman degradation and analyses of molecular masses of the peptides generated by two enzymatic cleavages performed independently, digestions with lysylendopeptidase and Endoproteinase Asp-N, with ionspray mass spectrometry, the primary structure of the protein has been elucidated to be completely identical with that deduced from its DNA sequence. Comparison of the amino acid sequence of P. furiosus MAP (P.f. MAP) with those of other MAPs from Eukarya and Bacteria showed that the protein has a high degree of sequence homology in the stretches surrounding the five cobalt-binding residues fully preserved in all of MAPs determined so far, but P.f. MAP belongs to Type II because it has an extra long insertion of about 60 amino acid residues between the fourth and fifth cobalt-binding ligands, similar to MAPs from human and rat, and to Met-AP2 from Saccharomyces cerevisiae in comparison to Type I MAPs from Bacteria. Therefore, P.f. MAP seems to be rather close to those from Eukarya, although it is distinct in lacking the N-terminal extension of about 90-150 residues universally found in MAPs from Eukarya. These findings suggest that P.f. MAP is evolutionally located at the Eukarya-Bacteria boundary. The enzyme expressed in E. coli exhibits a considerable thermostability, with a half-life of approximately 4.5 h at 90.degree.C and an optimum temperature of around 90.degree.C.

L37 ANSWER 34 OF 64 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

AB A full-length recombinant human apolipoprotein C-II (ApoC-II) has been successfully expressed in Escherichia coli using the T7 expression system. The recombinant ApoC-II, which was expressed intracellularly in the inclusion bodies, was solubilized with 8 M urea and purified using Sephadex G-75 gel permeation chromatography. Four liters of the bacterial culture yielded 16-20 mg of purified recombinant ApoC-II. Sequencing and mass spectrometric analyses indicated that the isolated recombinant ApoC-II contained predominantly (64%) the native form with threonine as the N-terminus, but also contained a minor (36%) molecular form of ApoC-II with an additional methionine at the N-terminus (Met-ApoC-II), Analysis of the recombinant ApoC-II by tryptic digestion and high performance liquid chromatography-electrospray mass spectrometry provides additional conclusive evidence that, with the exception of the N-terminus of Met-ApoC-II, the expressed ApoC-II has the expected peptide sequence. However, this extra N-terminal methionine residue can be excised by further in vitro treatment with **methionine aminopeptidase**. The purified recombinant ApoC-II was found to be competent in the activation of bovine milk lipoprotein lipase. Thus, the recombinant ApoC-II prepared from E. coli may have a pharmacological application for the treatment of patients with genetic hypertriglyceridemia caused by ApoC-II deficiency.

L37 ANSWER 42 OF 64 MEDLINE on STN

AB Human immunodeficiency virus (HIV) reverse transcriptase isolated from viral particles contains two subunits, p51 and p66. We have produced both subunits in separate Escherichia coli strains using expression vectors. Stop codons were placed immediately after the codon for the carboxyl-terminal residue of the mature processed p51 and p66 subunits found in viral particles. Insertion of a methionine in front of the HIV protease cleavage site in the recombinant protein enabled synthesis of both subunits with the natural amino-terminal proline, since E. coli **methionine aminopeptidase** cleaves a Met-Pro amino-terminal linkage. That this occurred to an extent greater than 95% was confirmed by sequencing the purified subunits. Examination of the activities of the individual p51 and p66 subunits on a variety of templates and under solution conditions optimized for each subunit revealed a significant catalytic activity for the natural p51 subunit. This result contrasts to results reported earlier for many recombinant forms without the natural amino and/or carboxyl termini. As expected from earlier work, the optimal homopolymeric template for the p66 subunit was poly(rA). For the p51 subunit, poly(dC) was found to be the optimal template; its activity is 2- to 4-fold greater than p66 on poly(dC). The p51 subunit is 13- to 50-fold less active on poly(rC). These findings are discussed in the context of our earlier hypothesis (McHenry, C. S. (1989) in Molecular Biology of Chromosome Function (Adolph, K., ed) Chap. 5, Springer-Verlag, New York) that the HIV reverse transcriptase might be functionally asymmetric with distinct plus- and minus-strand polymerases.

L37 ANSWER 43 OF 64 MEDLINE on STN DUPLICATE 16

AB We have constructed a plasmid (pHE2) in which the synthetic human alpha- and beta-globin genes and the **methionine aminopeptidase** (Met-AP) gene from Escherichia coli are coexpressed under the control of separate tac promoters. The Hbs were expressed in E. coli JM109 and purified by fast protein liquid chromatography, producing two major components, a and b. Electrospray mass spectrometry shows that at least 98% and about 90% of the expressed alpha and beta chains of component a, respectively, have the expected masses. The remaining 10% of the beta chain in component a corresponds in mass to the beta chain plus methionine. In component b, both alpha and beta chains have the correct masses without detectable N-terminal methionine (< 2%). These results have been confirmed by Edman degradation studies of the amino-terminal sequences of the alpha and beta chains of these two recombinant Hb (rHb)

samples. rHbs from components a and b exhibit visible optical spectra identical to that of human normal adult Hb (Hb A). Component a and Hb A have very similar oxygen-binding properties, but component b shows somewhat altered oxygen binding, especially at low pH values. 1H-NMR spectra of component a and Hb A are essentially identical, whereas those of component b exhibit altered ring current-shifted and hyperfine-shifted proton resonances, indicating altered heme conformation in the beta chain. These altered resonance patterns can be changed to those of Hb A by converting component b to the ferric state and then to the deoxy state and finally back to either the carbonmonoxy or oxy form. Thus, our E. coli expression system produces native, unmodified Hb A in high yield and can be used to produce desired **mutant** Hbs.

=> d ab 47,48,50,52,56-61

L37 ANSWER 47 OF 64 MEDLINE on STN DUPLICATE 17
AB A **methionine aminopeptidase** that specifically removes methionine residues from peptides with amino-terminal sequences of Met-Ala-, Met-Val-, Met-Ser-, Met-Gly-, and Met-Pro- but not Met-Leu- or Met-Lys- has been isolated to homogeneity from porcine liver by a procedure involving five chromatographic steps. The enzyme, whose specificity matches that predicted for the entity responsible for the co-translational amino-terminal processing of nascent polypeptide chains, has a measured molecular mass of 70,000 Da by SDS-polyacrylamide electrophoresis and 67,000 Da by gel chromatography (under nondenaturing conditions), suggesting the native molecule is a monomer. It is activated by Co2+ and inhibited by beta-mercaptoethanol and EDTA. With octapeptide substrates related to the amino-terminal portion of the beta-chain of human hemoglobin (with a histidine in position 3), the enzyme had a pH optimum of 6.0. With a synthetic peptide devoid of histidine, it showed no pH dependence from 6.0 to 8.0. This sensitivity may be due to the propensity of peptides with histidine in the third position to bind divalent cations such as Co2+. The measured Km and kappa cat values were affected by residues in the second position. The peptide corresponding to the natural sequence (Met-Val-His-) gave a kappa cat/Km value of 260 mM-1 s-1; substitution of alanine in the second position raised the kappa cat/Km to 1523 mM-1 s-1, but substitution of proline lowered the value to 130. The effects are primarily on the kappa cat. The substitution of proline (for histidine) in the third position, the **mutation** found in hemoglobin Long Island, prevents the removal of the methionine residue, as occurs with the **mutant** protein. The porcine liver enzyme is similar to **methionine aminopeptidases** isolated from Escherichia coli, Salmonella typhimurium, and yeast in that it also is stimulated by Co2+. However, it is much larger than these enzymes and differs somewhat in specificity, particularly with the yeast enzyme.

L37 ANSWER 48 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
AB A yeast gene for a **methionine aminopeptidase**, one of the central enzymes in protein synthesis, was cloned and sequenced. The DNA sequence encodes a precursor protein contg. 387 amino acid residues. The mature protein, whose NH2-terminal sequence was confirmed by Edman degrdn., consists of 377 amino acids. The function of the 10-residue sequence at the NH2 terminus, contg. 1 serine and 6 threonine residues, remains to be established. In contrast to the structure of the prokaryotic enzyme, the yeast **methionine aminopeptidase** consists of 2 functional domains: a unique NH2-terminal domain contg. 2 motifs resembling zinc fingers, which may allow the protein to interact with ribosomes, and a catalytic COOH-terminal domain resembling other prokaryotic **methionine aminopeptidases**. Furthermore, unlike the case for the prokaryotic gene, the deletion of the yeast MAP1 gene is not lethal, suggesting for the first time that alternative NH2-terminal processing pathway(s) exist for cleaving methionine from

nascent polypeptide chains in eukaryotic cells.

L37 ANSWER 50 OF 64 MEDLINE on STN DUPLICATE 18
AB A synthetic gene encoding the Group II phospholipase A2 (PLA2) from the venom of Agkistrodon piscivorus piscivorus has been constructed and expressed with high efficiency in Escherichia coli. No enzymatic activity was recovered when the polypeptide contained the initiator Met residue. Replacement of an Asn residue penultimate to the initiator Met with Ser or Gly permitted removal of the initiator Met by the endogenous **methionine aminopeptidase**. The amino-terminal serine (N-Ser) and amino-terminal glycine PLA2's were isolated from intracellular inclusion bodies and were renatured with 25% recovery. Automated Edman degradation confirmed the removal of the initiator Met and confirmed the sequence of the first 40 residues of N-Ser PLA2. The recombinant proteins were purified to apparent homogeneity and showed the same specific activity as the wild-type protein. N-Ser PLA2 demonstrated the same kinetics of activation as the wild type enzyme on large vesicles of zwitterionic lipid.

L37 ANSWER 52 OF 64 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
AB Genetic engineering can complement traditional methods to improve fermentation processes with the aim of reducing production costs. Selected examples in which genetic engineering techniques were used to improve fermentation processes were described. Example 1: fermentation of corn starch to ethanol, where the fermentation rate of soluble starch by recombinant Saccharomyces cerevisiae strains containing the Aspergillus awamori glucoamylase (EC-3.2.1.3) gene was controlled by the glucoamylase activity. Improved rates of starch fermentation were achieved using recombinant strains utilizing maltose and possessing a higher glucoamylase activity. Example 2: removal of the initiation methionine from recombinant proteins using **methionine-aminopeptidase** produced by recombinant Escherichia coli. Example 3: higher expression of recombinant proteins with low acetic acid producing **mutants** due to higher cell density fermentations, higher production rates and increased product concentration. Example 4: genetic methods to improve cellulose production by Acetobacter **mutants** defective in glucose-dehydrogenase (EC-1.1.1.47). (3 ref)

L37 ANSWER 56 OF 64 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
AB A human granulocyte colony stimulating factor (CSF) gene was cloned in Escherichia coli MM294 using plasmid pHCW701 (containing a trpP promoter, to generate plasmid pPD2), or plasmid pFC54.t (containing a pL promoter, to generate plasmid pJD1) as expression vector. Expression in E. coli was improved by alteration of the 5' sequence of the gene by site-directed **mutagenesis**. Initially, no mRNA or protein was detected in the trpP system, and only mRNA was detected in the pL system. When the G+C content was decreased at the 5' end, without altering the predicted protein sequence, mRNA and protein were detected in both systems. Expression reached 17% and 6.5% of total soluble cellular protein in the pL and trpP expression systems, respectively. The N-terminal sequence of the recombinant granulocyte CSF from the pL system was Met-Thr-Pro-Leu-Gly-Pro. Granulocyte CSF isolated from a human LD-1 cell culture did not have an N-terminal methionine residue. Deletion of the threonine codon at the start of the gene for the mature protein resulted in efficient removal of the methionine residue during expression in E. coli. (34 ref)

L37 ANSWER 57 OF 64 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
AB A 3.5 kbp PstI fragment carrying the whole gene coding for the Escherichia coli **methionine-aminopeptidase** (map) which contains 2.3 kbp of the 5' region was cloned. A total PstI genomic digest of C600 DNA (30 ug) was electrophoresed on an agarose gel. Fragments of 3-4.5 Kbp were electroeluted from gel slices and ligated to

PstI-cut replicative form of M13mp19. Standard hybridizing procedures were used to identify plaques hybridizing with a synthetic 30-mer oligonucleotide probe corresponding to the first 10 codons of map. Recombinant phages were 50% larger than the wild-type M13mp19 phages and were stable. Oligonucleotide hybridization provides a very efficient way to clone homologous genes in E. coli JM105 when a partial amino acid sequence of the product is known, particularly when no characterized **mutation** can be used in a complementation test. (8 ref)

L37 ANSWER 58 OF 64 MEDLINE on STN DUPLICATE 21
AB Polypeptides synthesized in the cytoplasm of eukaryotes are generally initiated with methionine, but N-terminal methionine is absent from most mature proteins. Many proteins are also N alpha-acetylated. The removal of N-terminal methionine and N alpha-acetylation are catalyzed by two enzymes during translation. The substrate preferences of the **methionine aminopeptidase** (EC 3.4.11.x) and N alpha-acetyltransferase (EC 2.3.1.x) have been partially inferred from the distribution of amino-terminal residues and/or **mutations** found for appropriate mature proteins, but with some contradictions. In this study, a synthetic gene corresponding to the mature amino acid sequence of the plant protein thaumatin, expressed in yeast as a nonexported protein, i.e., lacking a signal peptide, has been used to delineate the specificities of these enzymes with respect to the penultimate amino acid. Site-directed **mutagenesis**, employing synthetic oligonucleotides, was utilized to construct genes encoding each of the 20 amino acids following the initiation methionine codon, and each protein derivative was isolated and characterized with respect to its amino-terminal structure. All four possible N-terminal variants--those with and without methionine and those with and without N alpha-acetylation--were obtained. These results define the specificity of these enzymes in situ and suggest that the nature of the penultimate amino-terminal residue is the major determinant of their selectivity.

L37 ANSWER 59 OF 64 HCAPLUS COPYRIGHT 2003 ACS on STN
AB Crude exts. of a multiply peptidase-deficient strain of S. typhimurium contain an aminopeptidase that specifically removes N-terminal methionine from peptides. This activity shows pronounced specificity for the peptide's 2nd amino acid; methionine is removed from peptides with alanine, threonine, or glycine in the 2nd position but not from those in which the 2nd amino acid is leucine or methionine. The activity is stimulated by Co2+ and is inhibited by EDTA. **Mutations** that lead to overprodn. (up to 30-fold) of the activity were obtained by selecting for growth on Met-Gly-Gly as a methionine source. These **mutations** map at .apprx.3 map units, and are phage P22 cotransducible with leu. The overproducer **mutations** are dominant to wild type, and duplication of the wild-type allele of the locus leads to a gene dosage effect on peptidase levels. This suggests that the locus of the overproducer **mutations** may be the structural gene for the peptidase. SDS-PAGE shows an increased level of a single protein of 34 kilodaltons in the overproducer **mutant**. This protein is highly enriched in a purified prepn. of the peptidase. The specificity of this enzyme suggests that it is involved in the cleavage of methionine from newly synthesized peptide chains. Treatment of purified unprocessed interleukin 1.beta. (contg. N-terminal methionine) with the purified peptidase results in removal of N-terminal methionine with no addnl. alterations. Thus N-terminal processing of at least this protein can occur after translation is complete. This enzyme was named peptidase M (methionine-specific aminopeptidase).

L37 ANSWER 60 OF 64 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
AB Computer analyses of about 100 chemically determined amino-terminal sequences of Escherichia coli proteins allowed the classification of N-terminal sequences into 2 categories, corresponding to processed and non-processed polypeptide chains. From this analysis, a molecular

enzymatic model was deduced, accounting for the occurrence or non-occurrence of the maturation proces, and consistent with the existence of a unique enzyme. According to the model, the excision of the initiator methionyl residue would take place only when the accessible area of the lateral chain of the 2nd amino acid is inferior to 147 Az. To examine the model, systematic substitution was performed on the 2nd amino acid of methionyl-tRNA-synthetase (EC-6.1.1.10) by site-directed **mutagenesis**. A shuttle vector based on protein fusion with beta-galactosidase was designed to facilitate rapid **mutant** protein purification and N-terminal microsequencing. Experimental results were in agreement with the proposed model, and confirmed prediction based on the model concerning amino acids not yet found in the 2nd position in bacterial proteins. (0 ref)

L37 ANSWER 61 OF 64 MEDLINE on STN DUPLICATE 22

AB Amino-terminal processing in the yeast Saccharomyces cerevisiae has been investigated by examining numerous **mutationally** altered forms of iso-1-cytochrome c. Amino-terminal residues of methionine were retained in sequences having penultimate residues of arginine, asparagine, glutamine, isoleucine, leucine, lysine, and methionine; in contrast, the amino-terminal methionine residues were exercised from residues of alanine, glycine, and threonine and were partially excised from residues of valine. The results suggest the occurrence of a yeast aminopeptidase that removes amino-terminal residues of methionine when they precede certain amino acids. A systematic search of the literature for amino-terminal sequences formed at initiation sites suggests the hypothetical yeast aminopeptidase usually has the same specificity as the amino peptidase from bacteria and higher eukaryotes. Our results and the results from the literature search suggest that the aminopeptidase cleaves amino-terminal methionine when it precedes residues of alanine, glycine, proline, serine, threonine, and valine but not when it precedes residues of arginine, asparagine, aspartic acid, glutamine glutamic acid, isoleucine, leucine, lysine, or methionine. In contrast to the normal iso-1-cytochrome c and in contrast to the majority of the **mutationally** altered proteins, certain forms were acetylated including the following sequences: acetyl(Ac)-Met-Ile-Arg-, Ac-Met-Ile-Lys, Ac-Met-Met-Asn-, and Ac-Met-Asn-Asn-. We suggest yeast contains acetyltransferases that acetylates these **mutant** forms of iso-1-cytochromes c because their amino-terminal regions resemble the amino-terminal regions of natural occurring proteins which are normally acetylated. The lack of acetylation of closely related sequences suggest that the hypothetical acetyltransferases are specific for certain amino-terminal sequences and that the 3 amino-terminal residues may play a critical role in determining these specificities.

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